02-16-07

Attorney Docket No. 18247-505

Express Mail Label No.: EV978767174US Date of Deposit: February 14, 2007

FEB 1.5 2007

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:

Lee

SERIAL NUMBER:

10/027,186

EXAMINER:

Shengjun Wang

PATENT NUMBER:

7,037,906 B1

ISSUE DATE:

May 2, 2006

FILING DATE:

December 20, 2001

ART UNIT:

1614

For:

METHODS FOR MODULATING TUMOR GROWTH AND METASTASIS

Certificate of Corrections Branch

ATTN: Marietta Joyce Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Certificate

FEB 2 % 2007

of Correction

## TRANSMITTAL LETTER

1. Request for Certificate of Correction of Letters Patent (6 pages);

2. Certificate of Correction (4 pages); and

3. Return Postcard.

In connection with the foregoing matter, please charge any fees that may be due to Deposit Account Number 50-0311, Reference No. 18217-505. A duplicate copy of this letter is provided for this purpose.

Respectfully submitted,

Keg No 58; 032

for

Ivor R. Elrifi, Reg. No. 39,529

Naomi S. Biswas, Reg. No. 38,384

Attorneys for Applicants Telephone (617) 542-6000

Facsimile: (617) 542-2241

Customer No. 30623

Dated: February 14, 2007

TRA 2255422v.1

Exgress Mail Label No.: EV978767174US Date of Deposit: February 14, 2007

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:

Lee

SERIAL NUMBER:

10/027,186

EXAMINER:

Shengjun Wang

PATENT NUMBER:

FEB 1 5 2007

7,037,906 B1

ISSUE DATE:

May 2, 2006

FILING DATE:

December 20, 2001

ART UNIT:

1614

FOR:

METHODS FOR MODULATING TUMOR GROWTH AND METASTASIS

Certificate of Corrections Branch

ATTN: Marietta Joyce Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

## REQUEST FOR CERTIFICATE OF CORRECTION OF LETTERS PATENT

- 1. Attached, in duplicate, is Form PTO-1050, with at least one copy being suitable for printing.
- 2. The correction in the References Cited section at page 1, field 56, the field does not contain the references cited in the Information Disclosure Statement Form 1449.

The References Cited field should include the following references:

4,940,726 07/10/90 Pettit, et al.

4,996,237 02/26/91 Pettit, et al.

5,409,953 04/25/95 Pettit, et al.

5,561,122 10/01/96 Pettit

5,569,786 10/29/96 Pettit, et al.

5,661,143 08/26/97 D'Amato, et al

6,342,219 01/29/02 Thorpe, et al.

WO 99/35150 Arizona Board of Regents 07/15/1999

WO 00/48590 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 00/48591 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 94/05682 Pelizzoni 03/17/1994

Issued: May 2, 2006

WO 01/74368 Angiogene Pharmaceuticals Ltd. 10/11/2002

WO 02/09700 Cancer Research Ventures Ltd. 02/07/2002

WO 02/34244 Aventis Pharma 05/02/2002

EP 1 068 870 Ajinomoto Co. Inc. 01/17/2001

Pettit and Rhodes (1998). "Antineoplastic Agents 389. New Syntheses of the combretastatin A-4 prodrug" Anti-Cancer Drug Design 13: 183-191.

Petit, et al. (1995). "Antineoplastic Agents 291. Isolation and Synthesis of Combretastatins A-4, A-5 and A-61a" J. Med. Chem. 38: 1666-1672.

Crombie, et al. (1979). "Isolation of Cannabispiradienone and Cannabidihydrophenantherene. Biosynthetic Relationships Between the spirans and dihydrostilbenes of Thailand Cannabis" *Tetrahedron Letts.* 7: 661-664.

Majumder and Joardar. (1984). "Structure of Erianin, a New Bibenzyl Derivative from the Orchid *Eria carinata*" *Indian J. Chem.* 23B: 1040-1042.

Fürstner and Nikolakis (1996). "Ethynylation of Aryl Halides by a Modified Suzuki Reaction: Application to the Synthesis of Combretastatin A-4, A-5 and Lunularic Acid" *Liebigs Ann.* Pgs. 2107-2113.

Remick, et al. (2000). "A Phase I Pharmacokinetic (PK) Study of Single Dose Intravenous (IV) Combretatstain A4 Prodrug (CA4P) in Patients (PTS) With Advanced Cancer" ASCO Presentation. New Orleans May 23 2000

Stevenson, et al. (2000). "Phase I/Pharmacokinetic trial of the endothelial toxin combretastatin A4P (CA4P) administered as an IV bolus on a daily x5 schedule every 21 days" ACCR San Francisco, CA.

Rustin, et al. (1999). "Combretastatin A4 phosphate (CA4P) selectively targets vasculature in animal and human tumors." *Proceedings of the 1999 AACR-NCI-EORT International Conference*. Mount Vernon Hospital, Northwood Middlesex UK. Abstract 16.

Galbralth, et al. (1999). "Quantitative analysis of endothelial cell shape change after treatment with combretastatin A4 phosphate." *AACR-NCI-EORTC International Conference*. Tumor Microcirculation Group, Gray Laboratory Cancer Research Trust, Northwood, UK. Abstract 399.

J. Randal, et al. (2000). "Antiangiogenesis Drugs Target Specific Cancers, Mechanisms." J. National Cancer Institute 92(7): 520-522.

OXIGENE Announces Promising Clinical Results for Lead Tumor Vascular Targeting Agent, Combretastatin A4 Prodrug. Press Release.

OXIGENE Signs Letter of Intent with Bristol-Myers Squibb for the Development and Commercialization of Combretastatin. Press Release (22 November 1999). pages 1-2.

Bristol-Myers Squibb/Oxigene HEALTH-NEWS-Daily (23 November 1999). Press Release.

Issued: May 2, 2006

OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE acquires rights to combretastatin. Reuters Medical News. (13 August 1999). Press Release

Bristol-Myers Squibb and OXIGENE Announce Research and Licensing Agreement for Anti-Tumor Agents. Press Release. Princeton New Jersey (16 December 1999) pgs.1-3.

Eikesdal, et al. (2000). "The new tubulin-inhibitor combretastatin A-4 enhances thermal damage in the BT4An rat glioma." *Int. J. Radiat. Oncol. Biol. Phys.* 46(3): 645-652. ABSTRACT

Chaplin, et al. (1999). "Anti-vascular approaches to solid tumor therapy: evaluation of combretastatin A4 phosphate." *Anticancer Research* 19(1A): 189-95. ABSTRACT

Grosios, et al. (1999). "In vivo and in vitro evaluation of combretastatin A-4 and its sodium phosphate prodrug." *British Journal of Cancer*. <u>81(8)</u>: 1318-27. ABSTRACT

Hori, et al. (1999). "Antitumor effects due to irreversible stoppage of tumor tissue blood flow: evaluation of a novel combretastatin A-4 derivative, AC7700." *Japanese Journal of Cancer Research* 90(9): 1026-38. ABSTRACT.

Korbelik, et al. (1999). "Examples of adjuvant treatment enhancing the antitumor effect of photodynamic therapy." *Proc. SPIE-Int. Soc. Opt. Eng.* 3592: 65-72. ABSTRACT.

Nihei, et al. (1999). "A novel combretastatin A-4 derivative, AC-7700, shows marked antitumor activity against advanced solid tumors and orthotopically transplanted tumors." *Japanese Journal of Cancer Research.* 90(9): 1016-25. ABSTRACT.

Nihei, et al. (1999). "Evaluation of antivascular and antimitotic effects of tubulin binding agents in solid tumor therapy." *Jpn. J. Cancer Res.* 90(12): 1387-1386. ABSTRACT.

Tozer, et al. (1999). "Combretastatin A-4 phosphate as a tumor vascular-targeting agent: early effects in tumors and normal tissues." Cancer Research 59(7): 1626-34. ABSTRACT

Eikesdal, et al. (1999). "The importance of timing in thermochemotherapy with tubulin inhibitors." Eur. J. Cancer 35(4 Supp.): S105. ABSTRACT.

Koutcher, et al. (1999). "Combretastatin A-4 phosphate depletes tumor energy and enhances the effect of mitomycin C but not radiation in a murine mammary carcinoma." *Proc. Am. Assoc. Cancer Res.* 40(90 Meet. 6): 0197-016X. ABSTRACT.

Murata, et al. (1999). "Improving conventional cancer therapy by targeting tumor vasculature." *Br. J. Cancer* 80(2): 90. ABSTRACT.

Murata, et al. (1999). "Improving anti-cancer therapy by targeting the tumor vasculature with combrestatins." Eur. J. Cancer 35(4): \$179. ABSTRACT.

Siemann, et al. (1999). "Potentiation of chemotherapy by vascular targeting agents." *Br. J. Cancer* 80(Suppl. 2): 90. ABSTRACT.

Issued: May 2, 2006

Li, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 disodium phosphate: effects on radiation therapy." *International Journal of Radiation Oncology, Biology, Physics* 42(4): 899-903. ABSTRACT.

Siemann, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 prodrug enhances the antitumor treatment efficacy of cisplatin." *Proc. Am. Assoc. Cancer Res.* 39(89): 277-278. ABSTRACT.

Ohsumi, et al. (1999). "Synthesis and antitumor activities of amino acid prodrugs of amino-combretastatins." Anti-Cancer Drug Design 14:539-548.

Lin, et al. (1989). "Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: a Structure-Activity Study." *Molecular Pharmacology* 34:200-208.

Grosios, et al. (2000). "Combination Chemotherapy with Combretastatin A-4 Phosphate and 5-Fluorouracil in an Experimental Murine Colon Adenocarcinoma." *AntiCancer Res*. 20:229-234

OXiGENE Annual Report. Annual Meeting of Shareholders (May 26, 2000)

Jordon, et al. (1998). "Tubulin as a target for anticancer drugs: agents which interact with the mitotic spindle." *Med. Res. Rev.* 18(4):259-96. ABSTRACT.

Chaplin, et al. (1996). "Antivascular approaches to solid tumor therapy: evaluation of tubulin binding agents." *Proc. Annu. Meet. Am. Assoc. Cancer Res.* 37: A3009. ABSTRACT.

Chaplin, et al. (1996). "Antivascular approaches to solid tumour therapy: evaluation of tubulin binding agents." *British Journal of Cancer*. 74(Supplement 27): S-86-S88. ABSTRACT.

Remick (2000). ASCO Poster Presentation, Case Western Univ.

Galbraith (2001). "Combretastatin A4 Phosphate Reduces Tumor Blood Flow in Animals and Man, Demonstrated by MRI." ASCO ABSTRACT 278.

Rustin (2001). "Phase 1 Study of Weekly Intravenous Combretastatin A4 Phosphate (CA4P); Pharmacokinetics and Toxicity." ASCO ABSTRACT 392.

Anderson (2000). "Measurement of Tumour and Normal Tissue (NT) Perfusion by Positron Emission Tomography (PET) in the Evaluation of Antivascular Therapy: Results in the Phase 1 Study of Combretastatin A4 Phosphate (CA4P)." ASCO ABSTRACT 695.

Nelkin and Ball (2001). "Combretastatin A-4 and doxorubicin combination treatment is effective in a preclinical model of human medullary thyroid carcinoma." *Oncology Reports* 8:157-160.

Horsman, et al. (2000). "Combretastatin Novel Vascular Targeting Drugs for Improving Anti-Cancer Therapy." *Angiogenesis; From the Molecular to Integrative Pharmacology* pgs.311-323.

Griggs, et al. (2001). "Targeting tumour vasculature: the development of combretastatin A4" *The Lancet Oncology* 2:82-87.

Issued: May 2, 2006

Landuyt. (2001). "In Vivo Antitumor Effect of Vascular Targeting Combined with Either Ionizing Radiation or Anti-Angiogenesis Treatment." *Int. J. Radiation Oncology Biol. Phys.* 49(2):443-450.

Landuyt, et al. (2000). "Vascular targeting of solid tumours: a major 'inverse' volume-response relationship following combretastatin A-4 phosphate treatment of rat rhabdomyosarcomas" *European Journal of Cancer* 36: 1833-1843.

Dark, et al. (1997). "Combretastatin A-4, an Agent That Displays Potent and Selective Toxicity toward Tumor Vasculature" *Cancer Research* 57:1829-1834

Siemann, et al. (2000). "Targeting tumor blood vesels: an adjuvant strategy for radiation therapy" *Radiotherapy and Oncology* <u>57</u>: 5-12.

Siemann, et al. (2002). "Vascular Targeting Agents Enhance Chemotherapeutic Agent Activities In Solid Tumor Therapy" *Int. J. Canc.* 99: 1-6.

Pedley, et al. (2001). "Eradication of Colorectal Xenografts by Combined Radioimmunotherapy and Combretastatin A-4 3-O-Phosphate" *Cancer Res.* 61: 4716-4722.

#### 3. Please send the Certificate of Correction to:

Name:

Ivor R. Elrifi, Esquire

Address:

Mintz, Levin, Cohn, Ferris, Glovsky

and Popeo, P.C. One Financial Center Boston, MA 02111

Issued: May 2, 2006

### **REMARKS**

Applicants request this Certificate of Correction to correct an error in this issued patent. The issued patent issued with only the references cited by the Examiner on the face of the patent. References cited by Applicants and considered by the Examiner are not on the face of the patent but rather the face of the patent says, "See application file for complete search history."

Applicants have spoken to Marietta Joyce in the Certificate of Correction Branch regarding this correct. In accordance with 35 U.S.C. § 254, as this error was the result of a Patent and Trademark Office mistake, no fees are believed due in connection with this Request. Should the Certificates Branch wish to discuss Applicant's request, the Certificates Branch is invited to telephone the undersigned attorney at 617/542-6000.

In connection with the foregoing matter, please charge any fees that may be due to Deposit Account Number 50-0311, Reference No. 18217-505. A duplicate copy of this letter is provided for this purpose.

Respectfully subm

Ivor R. Elrifi, Reg. No. 39,529

Naomi S. Biswas, Reg. No. 38,384

Attorneys for Applicants Telephone (617) 542-6000

Facsimile: (617) 542-2241

Customer No. 30623

Dated: February 14, 2007

TRA 2255203v.1

Express Mail Label No.:

Date of Deposit: January 25, 2007

PTO/SB/44 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

(Also Form PTO-1050)

# UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO.:

7,037,906 B1

DATED:

May 2, 2006

**INVENTORS:** 

Francis Y. Lee

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below.

The References Cited section at page 1, field 56 does not contain the references cited in the Information Disclosure Statement Form 1449.

The References Cited field should include the following references:

4,940,726 07/10/90 Pettit, et al.

4,996,237 02/26/91 Pettit, et al.

5,409,953 04/25/95 Pettit, et al.

5,561,122 10/01/96 Pettit

5,569,786 10/29/96 Pettit, et al.

5,661,143 08/26/97 D'Amato, et al

6,342,219 01/29/02 Thorpe, et al.

WO 99/35150 Arizona Board of Regents 07/15/1999

WO 00/48590 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 00/48591 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 94/05682 Pelizzoni 03/17/1994

WO 01/74368 Angiogene Pharmaceuticals Ltd. 10/11/2002

WO 02/09700 Cancer Research Ventures Ltd. 02/07/2002

WO 02/34244 Aventis Pharma 05/02/2002

EP 1 068 870 Ajinomoto Co. Inc. 01/17/2001

Pettit and Rhodes (1998). "Antineoplastic Agents 389. New Syntheses of the combretastatin A-4 prodrug" *Anti-Cancer Drug Design* 13: 183-191.

Petit, et al. (1995). "Antineoplastic Agents 291. Isolation and Synthesis of Combretastatins A-4, A-5 and A-61a" J. Med. Chem. 38: 1666-1672.

Crombie, et al. (1979). "Isolation of Cannabispiradienone and

Cannabidihydrophenantherene. Biosynthetic Relationships Between the spirans and

dihydrostilbenes of Thailand Cannabis" Tetrahedron Letts. 7: 661-664.

Majumder and Joardar. (1984). "Structure of Erianin, a New Bibenzyl Derivative from the Orchid *Eria carinata*" *Indian J. Chem.* 23B: 1040-1042.

Fürstner and Nikolakis (1996). "Ethynylation of Aryl Halides by a Modified Suzuki Reaction: Application to the Synthesis of Combretastatin A-4, A-5 and Lunularic Acid" *Liebigs Ann.* Pgs. 2107-2113.

Remick, et al. (2000). "A Phase I Pharmacokinetic (PK) Study of Single Dose Intravenous (IV) Combretatstain A4 Prodrug (CA4P) in Patients (PTS) With Advanced Cancer" ASCO Presentation. New Orleans May 23 2000

Stevenson, et al. (2000). "Phase I/Pharmacokinetic trial of the endothelial toxin combretastatin A4P (CA4P) administered as an IV bolus on a daily x5 schedule every 21 days" ACCR San Francisco, CA.

Rustin, et al. (1999). "Combretastatin A4 phosphate (CA4P) selectively targets vasculature in animal and human tumors." *Proceedings of the 1999 AACR-NCI-EORT International Conference*. Mount Vernon Hospital, Northwood Middlesex UK. Abstract 16. Galbralth, et al. (1999). "Quantitative analysis of endothelial cell shape change after treatment with combretastatin A4 phosphate." *AACR-NCI-EORTC International Conference*. Tumor Microcirculation Group, Gray Laboratory Cancer Research Trust, Northwood, UK. Abstract 399.

J. Randal, et al. (2000). "Antiangiogenesis Drugs Target Specific Cancers, Mechanisms." J. National Cancer Institute 92(7): 520-522.

OXIGENE Announces Promising Clinical Results for Lead Tumor Vascular Targeting Agent, Combretastatin A4 Prodrug. Press Release.

OXIGENE Signs Letter of Intent with Bristol-Myers Squibb for the Development and Commercialization of Combretastatin. Press Release (22 November 1999). pages 1-2. Bristol-Myers Squibb/Oxigene HEALTH-NEWS-Daily (23 November 1999). Press Release. OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE acquires rights to combretastatin. Reuters Medical News. (13 August 1999). Press Release

Bristol-Myers Squibb and OXIGENE Announce Research and Licensing Agreement for Anti-Tumor Agents. Press Release. Princeton New Jersey (16 December 1999) pgs.1-3. Eikesdal, et al. (2000). "The new tubulin-inhibitor combretastatin A-4 enhances thermal damage in the BT4An rat glioma." *Int. J. Radiat. Oncol. Biol. Phys.* 46(3): 645-652. ABSTRACT

Chaplin, et al. (1999). "Anti-vascular approaches to solid tumor therapy: evaluation of combretastatin A4 phosphate." *Anticancer Research* 19(1A): 189-95. ABSTRACT Grosios, et al. (1999). "In vivo and in vitro evaluation of combretastatin A-4 and its sodium phosphate prodrug." *British Journal of Cancer*. 81(8): 1318-27. ABSTRACT Hori, et al. (1999). "Antitumor effects due to irreversible stoppage of tumor tissue blood flow: evaluation of a novel combretastatin A-4 derivative, AC7700." *Japanese Journal of Cancer Research* 90(9): 1026-38. ABSTRACT.

Korbelik, et al. (1999). "Examples of adjuvant treatment enhancing the antitumor effect of photodynamic therapy." *Proc. SPIE-Int. Soc. Opt. Eng.* 3592: 65-72. ABSTRACT.

Nihei, et al. (1999). "A novel combretastatin A-4 derivative, AC-7700, shows marked antitumor activity against advanced solid tumors and orthotopically transplanted tumors." *Japanese Journal of Cancer Research.* 90(9): 1016-25. ABSTRACT.

Nihei, et al. (1999). "Evaluation of antivascular and antimitotic effects of tubulin binding agents in solid tumor therapy." *Jpn. J. Cancer Res.* 90(12): 1387-1386. ABSTRACT.

Tozer, et al. (1999). "Combretastatin A-4 phosphate as a tumor vascular-targeting agent: early effects in tumors and normal tissues." Cancer Research 59(7): 1626-34. ABSTRACT Eikesdal, et al. (1999). "The importance of timing in thermochemotherapy with tubulin inhibitors." Eur. J. Cancer 35(4 Supp.): S105. ABSTRACT.

Koutcher, et al. (1999). "Combretastatin A-4 phosphate depletes tumor energy and enhances the effect of mitomycin C but not radiation in a murine mammary carcinoma." *Proc. Am. Assoc. Cancer Res.* 40(90 Meet. 6): 0197-016X. ABSTRACT.

Murata, et al. (1999). "Improving conventional cancer therapy by targeting tumor vasculature." *Br. J. Cancer* <u>80(2)</u>: 90. ABSTRACT.

Murata, et al. (1999). "Improving anti-cancer therapy by targeting the tumor vasculature with combrestatins." Eur. J. Cancer 35(4): S179. ABSTRACT.

Siemann, et al. (1999). "Potentiation of chemotherapy by vascular targeting agents." *Br. J. Cancer* 80(Suppl. 2): 90. ABSTRACT.

Li, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 disodium phosphate: effects on radiation therapy." *International Journal of Radiation Oncology, Biology, Physics* 42(4): 899-903. ABSTRACT.

Siemann, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 prodrug enhances the antitumor treatment efficacy of cisplatin." *Proc. Am. Assoc. Cancer Res.* 39(89): 277-278. ABSTRACT.

Ohsumi, et al. (1999). "Synthesis and antitumor activities of amino acid prodrugs of amino-combretastatins." Anti-Cancer Drug Design 14:539-548.

Lin, et al. (1989). "Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: a Structure-Activity Study." *Molecular Pharmacology* 34:200-208.

Grosios, et al. (2000). "Combination Chemotherapy with Combretastatin A-4 Phosphate and 5-Fluorouracil in an Experimental Murine Colon Adenocarcinoma." *AntiCancer Res.* 20:229-234

OXiGENE Annual Report. Annual Meeting of Shareholders (May 26, 2000)

Jordon, et al. (1998). "Tubulin as a target for anticancer drugs: agents which interact with the mitotic spindle." *Med. Res. Rev.* 18(4):259-96. ABSTRACT.

Chaplin, et al. (1996). "Antivascular approaches to solid tumor therapy: evaluation of tubulin binding agents." *Proc. Annu. Meet. Am. Assoc. Cancer Res.* 37: A3009. ABSTRACT. Chaplin, et al. (1996). "Antivascular approaches to solid tumour therapy: evaluation of tubulin binding agents." *British Journal of Cancer.* 74(Supplement 27): S-86-S88. ABSTRACT.

Remick (2000). ASCO Poster Presentation, Case Western Univ.

Galbraith (2001). "Combretastatin A4 Phosphate Reduces Tumor Blood Flow in Animals and Man, Demonstrated by MRI." ASCO ABSTRACT 278.

Rustin (2001). "Phase 1 Study of Weekly Intravenous Combretastatin A4 Phosphate (CA4P); Pharmacokinetics and Toxicity." ASCO ABSTRACT 392.

Anderson (2000). "Measurement of Tumour and Normal Tissue (NT) Perfusion by Positron Emission Tomography (PET) in the Evaluation of Antivascular Therapy: Results in the Phase 1 Study of Combretastatin A4 Phosphate (CA4P)." ASCO ABSTRACT 695. Nelkin and Ball (2001). "Combretastatin A-4 and doxorubicin combination treatment is effective in a preclinical model of human medullary thyroid carcinoma." Oncology Reports 8:157-160.

Horsman, et al. (2000). "Combretastatin Novel Vascular Targeting Drugs for Improving Anti-Cancer Therapy." Angiogenesis; From the Molecular to Integrative Pharmacology pgs.311-323.

Griggs, et al. (2001). "Targeting tumour vasculature: the development of combretastatin A4" *The Lancet Oncology* 2:82-87.

Landuyt. (2001). "In Vivo Antitumor Effect of Vascular Targeting Combined with Either Ionizing Radiation or Anti-Angiogenesis Treatment." *Int. J. Radiation Oncology Biol. Phys.* 49(2):443-450.

Landuyt, et al. (2000). "Vascular targeting of solid tumours: a major 'inverse' volume-response relationship following combretastatin A-4 phosphate treatment of rat rhabdomyosarcomas" *European Journal of Cancer* 36: 1833-1843.

Dark, et al. (1997). "Combretastatin A-4, an Agent That Displays Potent and Selective Toxicity toward Tumor Vasculature" *Cancer Research* 57:1829-1834

Siemann, et al. (2000). "Targeting tumor blood vesels: an adjuvant strategy for radiation therapy" *Radiotherapy and Oncology* <u>57</u>: 5-12.

Siemann, et al. (2002). "Vascular Targeting Agents Enhance Chemotherapeutic Agent Activities In Solid Tumor Therapy" *Int. J. Canc.* 99: 1-6.

Pedley, et al. (2001). "Eradication of Colorectal Xenografts by Combined Radioimmunotherapy and Combretastatin A-4 3-*O*-Phosphate" *Cancer Res.* <u>61</u>: 4716-4722.

MAILING ADDRESS OF SENDER:

Ivor R. Elrifi, Reg. No. 39,529 Attorney for Applicants MINTZ LEVIN One Financial Center Boston, Massachusetts 02111 Tel: (617) 542-6000

Fax: (617) 542-2241 Customer No. 30623

TRA 2247174v.1

Express Mail Label No.:

Date of Deposit: January 25, 2007

PTO/SB/44 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

(Also Form PTO-1050)

# UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO.:

7,037,906 B1

DATED:

May 2, 2006

**INVENTORS:** 

Francis Y. Lee

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below.

The References Cited section at page 1, field 56 does not contain the references cited in the Information Disclosure Statement Form 1449.

The References Cited field should include the following references:

4,940,726 07/10/90 Pettit, et al.

4,996,237 02/26/91 Pettit, et al.

5,409,953 04/25/95 Pettit, et al.

5,561,122 10/01/96 Pettit

5,569,786 10/29/96 Pettit, et al.

5,661,143 08/26/97 D'Amato, et al

6,342,219 01/29/02 Thorpe, et al.

WO 99/35150 Arizona Board of Regents 07/15/1999

WO 00/48590 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 00/48591 Angiogene Pharmaceuticals Ltd. 08/24/2000

WO 94/05682 Pelizzoni 03/17/1994

WO 01/74368 Angiogene Pharmaceuticals Ltd. 10/11/2002

WO 02/09700 Cancer Research Ventures Ltd. 02/07/2002

WO 02/34244 Aventis Pharma 05/02/2002

EP 1 068 870 Ajinomoto Co. Inc. 01/17/2001

Pettit and Rhodes (1998). "Antineoplastic Agents 389. New Syntheses of the combretastatin A-4 prodrug" *Anti-Cancer Drug Design* 13: 183-191.

Petit, et al. (1995). "Antineoplastic Agents 291. Isolation and Synthesis of Combretastatins A-4, A-5 and A-61a" J. Med. Chem. 38: 1666-1672.

Crombie, et al. (1979). "Isolation of Cannabispiradienone and

Cannabidihydrophenantherene. Biosynthetic Relationships Between the spirans and dihydrostilbenes of Thailand Cannabis" *Tetrahedron Letts.* 7: 661-664.

Majumder and Joardar. (1984). "Structure of Erianin, a New Bibenzyl Derivative from the Orchid *Eria carinata*" *Indian J. Chem.* 23B: 1040-1042.

Fürstner and Nikolakis (1996). "Ethynylation of Aryl Halides by a Modified Suzuki Reaction: Application to the Synthesis of Combretastatin A-4, A-5 and Lunularic Acid" *Liebigs Ann.* Pgs. 2107-2113.

Remick, et al. (2000). "A Phase I Pharmacokinetic (PK) Study of Single Dose Intravenous (IV) Combretatstain A4 Prodrug (CA4P) in Patients (PTS) With Advanced Cancer" ASCO Presentation. New Orleans May 23 2000

Stevenson, et al. (2000). "Phase I/Pharmacokinetic trial of the endothelial toxin combretastatin A4P (CA4P) administered as an IV bolus on a daily x5 schedule every 21 days" ACCR San Francisco, CA.

Rustin, et al. (1999). "Combretastatin A4 phosphate (CA4P) selectively targets vasculature in animal and human tumors." *Proceedings of the 1999 AACR-NCI-EORT International Conference*. Mount Vernon Hospital, Northwood Middlesex UK. Abstract 16. Galbralth, et al. (1999). "Quantitative analysis of endothelial cell shape change after treatment with combretastatin A4 phosphate." *AACR-NCI-EORTC International Conference*. Tumor Microcirculation Group, Gray Laboratory Cancer Research Trust, Northwood, UK. Abstract 399.

J. Randal, et al. (2000). "Antiangiogenesis Drugs Target Specific Cancers, Mechanisms." J. National Cancer Institute 92(7): 520-522.

OXIGENE Announces Promising Clinical Results for Lead Tumor Vascular Targeting Agent, Combretastatin A4 Prodrug. Press Release.

OXIGENE Signs Letter of Intent with Bristol-Myers Squibb for the Development and Commercialization of Combretastatin. Press Release (22 November 1999). pages 1-2. Bristol-Myers Squibb/Oxigene HEALTH-NEWS-Daily (23 November 1999). Press Release. OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE announces favorable phase I results for angiogenesis inhibitor. Reuters Medical News. (7 October 1999). Press Release.

OXIGENE acquires rights to combretastatin. Reuters Medical News. (13 August 1999). Press Release

Bristol-Myers Squibb and OXIGENE Announce Research and Licensing Agreement for Anti-Tumor Agents. Press Release. Princeton New Jersey (16 December 1999) pgs.1-3. Eikesdal, et al. (2000). "The new tubulin-inhibitor combretastatin A-4 enhances thermal damage in the BT4An rat glioma." *Int. J. Radiat. Oncol. Biol. Phys.* 46(3): 645-652. ABSTRACT

Chaplin, et al. (1999). "Anti-vascular approaches to solid tumor therapy: evaluation of combretastatin A4 phosphate." Anticancer Research 19(1A): 189-95. ABSTRACT Grosios, et al. (1999). "In vivo and in vitro evaluation of combretastatin A-4 and its sodium phosphate prodrug." British Journal of Cancer. 81(8): 1318-27. ABSTRACT Hori, et al. (1999). "Antitumor effects due to irreversible stoppage of tumor tissue blood flow: evaluation of a novel combretastatin A-4 derivative, AC7700." Japanese Journal of Cancer Research 90(9): 1026-38. ABSTRACT.

Korbelik, et al. (1999). "Examples of adjuvant treatment enhancing the antitumor effect of photodynamic therapy." *Proc. SPIE-Int. Soc. Opt. Eng.* 3592: 65-72. ABSTRACT.

Nihei, et al. (1999). "A novel combretastatin A-4 derivative, AC-7700, shows marked antitumor activity against advanced solid tumors and orthotopically transplanted tumors." *Japanese Journal of Cancer Research*. 90(9): 1016-25. ABSTRACT.

Nihei, et al. (1999). "Evaluation of antivascular and antimitotic effects of tubulin binding agents in solid tumor therapy." *Jpn. J. Cancer Res.* 90(12): 1387-1386. ABSTRACT.

Tozer, et al. (1999). "Combretastatin A-4 phosphate as a tumor vascular-targeting agent: early effects in tumors and normal tissues." Cancer Research 59(7): 1626-34. ABSTRACT Eikesdal, et al. (1999). "The importance of timing in thermochemotherapy with tubulin inhibitors." Eur. J. Cancer 35(4 Supp.): S105. ABSTRACT.

Koutcher, et al. (1999). "Combretastatin A-4 phosphate depletes tumor energy and enhances the effect of mitomycin C but not radiation in a murine mammary carcinoma." *Proc. Am. Assoc. Cancer Res.* 40(90 Meet. 6): 0197-016X. ABSTRACT.

Murata, et al. (1999). "Improving conventional cancer therapy by targeting tumor vasculature." *Br. J. Cancer* <u>80(2)</u>: 90. ABSTRACT.

Murata, et al. (1999). "Improving anti-cancer therapy by targeting the tumor vasculature with combrestatins." Eur. J. Cancer 35(4): S179. ABSTRACT.

Siemann, et al. (1999). "Potentiation of chemotherapy by vascular targeting agents." Br. J. Cancer 80(Suppl. 2): 90. ABSTRACT.

Li, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 disodium phosphate: effects on radiation therapy." *International Journal of Radiation Oncology, Biology, Physics* 42(4): 899-903. ABSTRACT.

Siemann, et al. (1998). "Targeting the tumor vasculature with combretastatin A-4 prodrug enhances the antitumor treatment efficacy of cisplatin." *Proc. Am. Assoc. Cancer Res.* 39(89): 277-278. ABSTRACT.

Ohsumi, et al. (1999). "Synthesis and antitumor activities of amino acid prodrugs of amino-combretastatins." Anti-Cancer Drug Design 14:539-548.

Lin, et al. (1989). "Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: a Structure-Activity Study." *Molecular Pharmacology* 34:200-208.

Grosios, et al. (2000). "Combination Chemotherapy with Combretastatin A-4 Phosphate and 5-Fluorouracil in an Experimental Murine Colon Adenocarcinoma." *AntiCancer Res.* 20:229-234

OXiGENE Annual Report. Annual Meeting of Shareholders (May 26, 2000)

Jordon, et al. (1998). "Tubulin as a target for anticancer drugs: agents which interact with the mitotic spindle." *Med. Res. Rev.* 18(4):259-96. ABSTRACT.

Chaplin, et al. (1996). "Antivascular approaches to solid tumor therapy: evaluation of tubulin binding agents." *Proc. Annu. Meet. Am. Assoc. Cancer Res.* 37: A3009. ABSTRACT. Chaplin, et al. (1996). "Antivascular approaches to solid tumour therapy: evaluation of tubulin binding agents." *British Journal of Cancer.* 74(Supplement 27): S-86-S88. ABSTRACT.

Remick (2000). ASCO Poster Presentation, Case Western Univ.

Galbraith (2001). "Combretastatin A4 Phosphate Reduces Tumor Blood Flow in Animals and Man, Demonstrated by MRI." ASCO ABSTRACT 278.

Rustin (2001). "Phase 1 Study of Weekly Intravenous Combretastatin A4 Phosphate (CA4P); Pharmacokinetics and Toxicity." ASCO ABSTRACT 392.

Anderson (2000). "Measurement of Tumour and Normal Tissue (NT) Perfusion by Positron Emission Tomography (PET) in the Evaluation of Antivascular Therapy: Results in the Phase 1 Study of Combretastatin A4 Phosphate (CA4P)." ASCO ABSTRACT 695. Nelkin and Ball (2001). "Combretastatin A-4 and doxorubicin combination treatment is effective in a preclinical model of human medullary thyroid carcinoma." Oncology Reports 8:157-160.

Horsman, et al. (2000). "Combretastatin Novel Vascular Targeting Drugs for Improving Anti-Cancer Therapy." *Angiogenesis; From the Molecular to Integrative Pharmacology* pgs.311-323.

Griggs, et al. (2001). "Targeting tumour vasculature: the development of combretastatin A4" *The Lancet Oncology* 2:82-87.

Landuyt. (2001). "In Vivo Antitumor Effect of Vascular Targeting Combined with Either Ionizing Radiation or Anti-Angiogenesis Treatment." *Int. J. Radiation Oncology Biol. Phys.* 49(2):443-450.

Landuyt, et al. (2000). "Vascular targeting of solid tumours: a major 'inverse' volume-response relationship following combretastatin A-4 phosphate treatment of rat rhabdomyosarcomas" *European Journal of Cancer* 36: 1833-1843.

Dark, et al. (1997). "Combretastatin A-4, an Agent That Displays Potent and Selective Toxicity toward Tumor Vasculature" *Cancer Research* <u>57</u>:1829-1834

Siemann, et al. (2000). "Targeting tumor blood vesels: an adjuvant strategy for radiation therapy" *Radiotherapy and Oncology* <u>57</u>: 5-12.

Siemann, et al. (2002). "Vascular Targeting Agents Enhance Chemotherapeutic Agent Activities In Solid Tumor Therapy" *Int. J. Canc.* 99: 1-6.

Pedley, et al. (2001). "Eradication of Colorectal Xenografts by Combined Radioimmunotherapy and Combretastatin A-4 3-*O*-Phosphate" *Cancer Res.* <u>61</u>: 4716-4722.

MAILING ADDRESS OF SENDER:

Ivor R. Elrifi, Reg. No. 39,529 Attorney for Applicants MINTZ LEVIN One Financial Center Boston, Massachusetts 02111

Tel: (617) 542-6000 Fax: (617) 542-2241 Customer No. 30623

TRA 2247174v.1